TRADE SECRET

Study Title

H-28072: Acute Oral Toxicity Study in Rats - Up-and-Down Procedure

TEST GUIDELINES: U.S. EPA Health Effect Test Guidelines
OPPTS 870.1100 (2002)

OECD Guideline for the Testing of Chemicals
Section 4 (Part 425) (2001)

AUTHOR: Carol Carpenter, B.A.

STUDY COMPLETED ON: July 25, 2007

PERFORMING LABORATORY: E.I. du Pont de Nemours and Company
Haskell[SM] Laboratory for Health and Environmental Sciences
P.O. Box 50
Newark, Delaware 19714
U.S.A.

LABORATORY PROJECT ID: DuPont-22932

WORK REQUEST NUMBER: 17199

SERVICE CODE NUMBER: 834

SPONSOR: E.I. du Pont de Nemours and Company
Wilmington, Delaware 19898
U.S.A.

GOOD LABORATORY PRACTICE COMPLIANCE STATEMENT

This study was conducted in compliance with U.S. EPA TSCA (40 CFR part 792) Good Laboratory Practice Standards, which are compatible with current OECD Good Laboratory Practices except for the item documented below. The item listed does not impact the validity of the study.

The test substance was characterized by the sponsor prior to the initiation of this study. Although the characterization was not performed under Good Laboratory Practice Standards, the accuracy of the data is considered sufficient for the purposes of this study. However, the test substance was subsequently characterized under Good Laboratory Standards; the Certificate of Analysis is included in this report.

Study Director: Carol Carpenter 25-July-2007

Carol Carpenter, B.A.
Senior Staff Toxicologist

Date

QUALITY ASSURANCE STATEMENT

Work Request Number: 17199
Service Code Number: 834

Key inspections for DuPont work request 17199, service code 834 were completed by the Quality Assurance Unit of DuPont and the findings were submitted on the following dates.

Phase Audited	***Audit Dates***	***Date Reported to Study Director***	***Date Reported to Management***
Protocol:	March 13, 2007	March 14, 2007	March 14, 2007
Conduct:	March 21, 2007	March 21, 2007	March 21, 2007
Report/Records:	May 25, 2007 July 24, 2007	May 25, 2007 July 24, 2007	May 25, 2007 July 24, 2007

Reported by: _____ 24 July 2007
Molly A. Butler
Quality Assurance Auditor
Date

CERTIFICATION

We, the undersigned, declare that this report provides an accurate evaluation of data obtained from this study.

Anatomic Pathology Evaluation Reported by: Lisa J. Lewis — 24-July-2007
Lisa J. Lewis
Associate Scientist
Date

Anatomic Pathology Evaluation Reviewed by: Steven R. Frame — 25 July 2007
Steven R. Frame, D.V.M., Ph.D., Diplomate A.C.V.P.
Research Fellow and Manager
Date

Reviewed by: Denise Hoban — 25 July 2007
Denise Hoban, B.A., MLT (ASCP)
Staff Medical Technologist and Supervisor
Date

Issued by Study Director: Carol Carpenter — 25-July-2007
Carol Carpenter, B.A.
Senior Staff Toxicologist
Date

TABLE OF CONTENTS

Page

GOOD LABORATORY PRACTICE COMPLIANCE STATEMENT 2

QUALITY ASSURANCE STATEMENT 3

CERTIFICATION 4

STUDY INFORMATION 6

SUMMARY 7

INTRODUCTION 8

MATERIALS AND METHODS 8
A. Test Guidelines 8
B. Test Substance 8
C. Test System 8
D. Animal Husbandry 8
E. Dosing 9
F. Observations, Body Weights, and Anatomic Pathology 10

RESULTS AND DISCUSSION 11

In-life Toxicology 11
A. Dose Progression and Mortality 11
B. Body Weights 12
C. Clinical Signs 12

Anatomic Pathology Evaluation 12
A. Gross Observations 12

CONCLUSIONS 12

RECORDS AND SAMPLE STORAGE 12

APPENDICES 13
Appendix A Certificate of Analysis 14
Appendix B Individual Body Weights 16
Appendix C Individual Body Weight Gains 19
Appendix D Individual Clinical Observations and Mortality Records 21
Appendix E Individual Animal Gross Observations 31

STUDY INFORMATION

Substance Tested:
- HFPO Dimer Acid Ammonium Salt
- 2,3,3,3-tetrafluoro-2-(heptafluoropropoxy)propionic acid, ammonium salt
- 62037-80-3 (CAS Number)
- H-28072

Haskell Number: 28072

Composition:

82.6%	Ammonium 2,3,3,3-tetrafluoro-2-(heptafluoropropoxy)propionate*
13.9%	Water
3.5%	Ammonium

* Note: The Ammonium-2,3,3,3-tetrafluoro-2-(heptafluoropropoxy) propionate component (AKA HFPO Dimer ammonium salt) contains 0.1 ppm HFPO trimer ammonium salt.

Purity: See composition, above

Physical Characteristics: Clear and colorless concentrated aqueous solution

Study Initiated/Completed: March 8, 2007 / (see report cover page)

Experimental Start/Termination: March 14, 2007 / July 25, 2007

SUMMARY

A single dose of H-28072 was administered by oral gavage to 1 fasted female rat each at a dose of 175 or 550 mg/kg, to 3 fasted female rats at a dose of 1750 mg/kg, and to 3 fasted female rats at a dose of 5000 mg/kg. The rats were dosed one at a time at a minimum of 48-hour intervals. The rats were observed for mortality, body weight effects, and clinical signs for up to 14 days after dosing. All rats were necropsied to detect grossly observable evidence of organ or tissue damage.

The 3 rats dosed at 5000 mg/kg were found dead on the day of dosing, 1 day after dosing, or 2 days after dosing. Clinical signs were observed in all rats and included hair loss, high posture, stained fur/skin, wet fur, lethargy, clear ocular discharge, prostrate posture, partially closed eyes, and/or salivation. With the exception of hair loss, no clinical signs were observed after day 2. No body weight losses occurred after dosing.

Gross findings were present in 3 rats dosed at 5000 mg/kg. These included: lung discoloration in rat 1651 (found dead); discoloration of the lungs and mandibular lymph nodes in rat 1746 (found dead); and discoloration of the lungs and liver in rat 1975 (found dead). No other gross findings were observed.

Under the conditions of this study, the oral LD_{50} for H-28072 was 3129 mg/kg for female rats.

In accordance with the provisions of Directive 67/548/EEC, classification is not required based on the results of this study.

INTRODUCTION

The purpose of this study was to assess the acute oral toxicity of H-28072 when administered by oral gavage to female rats. Per the test guidelines, the starting dose level of 175 mg/kg was chosen based on available toxicity data for this test substance.

MATERIALS AND METHODS

A. Test Guidelines

The study design complied with the following test guidelines:

- U.S. EPA, OPPTS 870.1100: Acute Oral Toxicity, *Health Effects Test Guidelines* (2002)
- OECD, Section 4 (Part 425): Acute Oral Toxicity – Up-and-Down Procedure, *Guideline for the Testing of Chemicals* (2001)

B. Test Substance

(Appendix A)

The test substance, H-28072, was supplied by the sponsor. The test substance appeared to be stable under the conditions of the study. No evidence of instability, such as a change in color or physical state, was observed.

C. Test System

Female Crl:CD(SD) rats were received from Charles River Laboratories, Inc., Raleigh, North Carolina.

The Crl:CD(SD) rat was selected based on consistently acceptable health status and on extensive experience with the strain at Haskell Laboratory.

D. Animal Husbandry

1. Housing

All animals were housed singly in stainless steel, wire-mesh cages suspended above cage boards.

2. Environmental Conditions

Animal rooms were maintained at a temperature of 18-26°C and a relative humidity of 30-70%. Animal rooms were artificially illuminated (fluorescent light) on an approximate 12-hour light/dark cycle. Any excursions outside of these ranges were of insufficient magnitude and/or duration to have adversely affected the validity of the study.

3. Feed and Water

PMI® Nutrition International, LLC Certified Rodent LabDiet® 5002 and water were available *ad libitum* except as noted in section E. Dosing.

4. Identification

Each rat was assigned an identification number which was recorded on a card affixed to the cage. The rats were tail-marked, using a water-insoluble marker, with the identification number.

5. Quarantine

The rats were weighed and observed for general health during the quarantine period (at least 6 days).

6. Animal Health and Environmental Monitoring Program

As specified in the Haskell Laboratory animal health and environmental monitoring program, the following procedures are performed periodically to ensure that contaminant levels are below those that would be expected to impact the scientific integrity of the study:

- Water samples are analyzed for total bacterial counts, and the presence of coliforms, lead, and other contaminants.
- Samples from freshly washed cages and cage racks are analyzed to ensure adequate sanitation by the cagewashers.

Certified animal feed is used, guaranteed by the manufacturer to meet specified nutritional requirements and not to exceed stated maximum concentrations of key contaminants, including specified heavy metals, aflatoxin, chlorinated hydrocarbons, and organophosphates. The presence of these contaminants below the maximum concentration stated by the manufacturer would not be expected to impact the integrity of the study.

The animal health and environmental monitoring program is administered by the attending laboratory animal veterinarian. Evaluation of these data did not indicate any conditions that affected the validity of the study.

E. Dosing

A single oral dose of H-28072 was administered neat by oral gavage to 1 fasted female rat each at a dose of 175 or 550 mg/kg, to 3 fasted female rats at a dose of 1750 mg/kg, and to 3 fasted female rats at a dose of 5000 mg/kg. The rats were dosed one at a time at a minimum of 48-hour intervals.

The rats were approximately 10 or 11 weeks old on the day of dosing. The rats were fasted approximately 16-18 hours prior to dosing, with food being returned to the rats approximately 3-4 hours after dosing. Individual dose volumes were calculated using the fasted body weights

obtained prior to dosing and the test substance density of 1.5308 g/mL. The test substance was stirred throughout the dosing procedure.

F. Observations, Body Weights, and Anatomic Pathology

Observations for mortality and signs of illness, injury, or abnormal behavior were made daily throughout the study. The rats were observed for clinical signs at the beginning of fasting, just before dosing (test day 0), once during the first 30 minutes after dosing and 2 more times on the day of dosing, and once each day thereafter. Rats were weighed on test days –1, 0, 7, and 14. On test day 14, the surviving rats were euthanized and necropsied to detect grossly observable evidence of organ or tissue damage. The rats were anesthetized by carbon dioxide and euthanized by exsanguination. The rats that died were also necropsied.

RESULTS AND DISCUSSION

In-life Toxicology

A. Dose Progression and Mortality

The dose progression and mortality are detailed below. The 3 rats dosed at 5000 mg/kg were found dead on the day of dosing, 1 day after dosing, or 2 days after dosing.

AOT425statpgm (Version: 1.0) Test Results and Recommendations
Acute Oral Toxicity (OECD Test Guideline 425) Statistical Program

Test type: Main Test
Limit dose (mg/kg): 5000
Assumed LD_{50} (mg/kg): Default
Assumed sigma (mg/kg): 0.5

Recommended dose progression: 5000, 1750, 550, 175, 55, 17.5, 5.5, 1.75 mg/kg

1. Data

Test Sequence	Animal ID	Dose (mg/kg)	Short-Term Result	Long-Term Result
1	1581	175	O	O
2	1585	550	O	O
3	1649	1750	O	O
4	1651	5000	X	X
5	1744	1750	O	O
6	1746	5000	X	X
7	1748	1750	O	O
8	1975	5000	X	X

X = Died
O = Survived

Dose Recommendation: The main test is complete.

Stopping criteria met: 5 reversals in 6 tests. Likelihood ratio criterion.

2. Summary of Long-Term Results

Dose (mg/kg)	O	X	Total
175	1	0	1
550	1	0	1
1750	3	0	3
5000	0	3	3
All Doses	5	3	8

Statistical Estimate based on long term outcomes: estimated LD_{50} = 3129 mg/kg (based on an assumed sigma of 0.5). Approximate 95% confidence interval is 1750 to 5000 mg/kg.

B. Body Weights

(Appendices B-C)

No body weight loss occurred after dosing.

C. Clinical Signs

(Appendix D)

Clinical signs were observed in all rats and included hair loss, high posture, stained fur/skin, wet fur, lethargy, clear ocular discharge, prostrate posture, partially closed eyes, and/or salivation. With the exception of hair loss, no clinical signs were observed after day 2.

Anatomic Pathology Evaluation

A. Gross Observations

(Appendix E)

Gross findings were present in 3 rats dosed at 5000 mg/kg. These included: lung discoloration in rat 1651 (found dead); discoloration of the lungs and mandibular lymph nodes in rat 1746 (found dead); and discoloration of the lungs and liver in rat 1975 (found dead). No other gross findings were observed.

CONCLUSIONS

Under the conditions of this study, the oral LD_{50} for H-28072 was 3129 mg/kg for female rats.

In accordance with the provisions of Directive 67/548/EEC, classification is not required based on the results of this study.

RECORDS AND SAMPLE STORAGE

Specimens (if applicable), raw data, the protocol, amendments (if any), and the final report will be retained at Haskell Laboratory, Newark, Delaware, or at Iron Mountain Records Management, Wilmington, Delaware.

APPENDICES

Appendix A
Certificate of Analysis

E. I. du Pont de Nemours and Company
Wilmington, DE 19898
USA

CERTIFICATE OF ANALYSIS

This Certificate of Analysis fulfills the requirement for characterization of a test substance prior to a study subject to GLP regulations. It documents the identity and content of the test substance. This work was conducted under EPA Good Laboratory Practice Standards (40 CFR 792).

Haskell Code Number	H-28072
Common Name	HFPO Dimer Acid Ammonium Salt
Purity Percent	82.6%
Other Components	Water – 13.9% Ammonium (excess) – 3.5%
Date of Analysis	July 19, 2007
Recommended reanalysis interval	1 year
Instructions for storage	NRT&H
Reference	DuPont-23285
Analysis performed at	E. I. DuPont de Nemours and Company DuPont Haskell Laboratories Newark, Delaware USA

Peter A. Bloxham, Ph.D.
Analyst's Name

Analyst's signature

23-JULY-2007
Date

Revision #1
July 20, 2007

Appendix B
Individual Body Weights

Individual Body Weights (g)

Group Sex	Animal Number	Bodyweights (g) Day numbers relative to Start Date -1	0	7	14
1f	1581	240.0	222.4	278.8	301.8

Group Sex	Animal Number	Bodyweights (g) Day numbers relative to Start Date -1	0	7	14
2f	1585	234.7	210.4	248.7	253.7

Group Sex	Animal Number	Bodyweights (g) Day numbers relative to Start Date -1	0	7	14
3f	1649	238.1	218.5	248.7	264.1

Group Sex	Animal Number	Bodyweights (g) Day numbers relative to Start Date -1	0	7	14
4f	1651	216.5	201.6	.	.

Nominal Dose: Group 1 – 175 mg/kg Group 2 – 550 mg/kg Group 3 – 1750 mg/kg
Group 4 – 5000 mg/kg Group 5 - 1750 mg/kg Group 6 – 5000 mg/kg
Group 7 – 1750 mg/kg Group 8 - 5000 mg/kg

Individual Body Weights (g)

Group Sex	Animal Number	Bodyweights (g) Day numbers relative to Start Date -1	0	7	14
5f	1744	238.0	220.8	243.9	257.2

Group Sex	Animal Number	Bodyweights (g) Day numbers relative to Start Date -1	0	7	14
6f	1746	241.7	220.3	.	.

Group Sex	Animal Number	Bodyweights (g) Day numbers relative to Start Date -1	0	7	14
7f	1748	231.5	212.4	238.7	244.4

Group Sex	Animal Number	Bodyweights (g) Day numbers relative to Start Date -1	0	7	14
8f	1975	234.1	213.8	.	.

Nominal Dose: Group 1 – 175 mg/kg Group 2 – 550 mg/kg Group 3 – 1750 mg/kg
Group 4 – 5000 mg/kg Group 5 - 1750 mg/kg Group 6 – 5000 mg/kg
Group 7 – 1750 mg/kg Group 8 - 5000 mg/kg

Appendix C
Individual Body Weight Gains

Individual Body Weight Gains (g)

	Days 0-7	Days 7-14	Days 0-14
Female, 175 mg/kg			
1581	56.4	23.0	79.4
Female, 550 mg/kg			
1585	38.3	5.0	43.3
Female, 1750 mg/kg			
1649	30.2	15.4	45.6
1744	23.1	13.3	36.4
1748	26.3	5.7	32.0

Appendix D
Individual Clinical Observations and Mortality Records

INDIVIDUAL CLINICAL OBSERVATIONS AND MORTALITY RECORDS

EXPLANATORY NOTES

ABBREVIATIONS:

ts1 - postdose observation 1 (within 30 minutes of dosing)
ts2 - postdose observation 2
ts3 - postdose observation 3

Individual Clinical Observations

Day numbers relative to Start Date

Group Sex	Animal Number	Clinical Sign	Site	-1 A	0 A	0 Ts1	0 Ts2	0 Ts3	1 A	2 A	3 A	4 A	5 A
1f	1581	No Abnormalities Detected		X	X	X	X	X	X	X	X	X	X
		Hair loss	Forelimb bilateral	.	.	.	.	.	.	.	.	.	.
		Scheduled sacrifice		.	.	.	.	.	.	.	.	.	.

(continued)

Group Sex	Animal Number	Clinical Sign	Site	6 A	7 A	8 A	9 A	10 A	11 A	12 A	13 A	14 A
1f	1581	No Abnormalities Detected		X	.	.	.	.	.	.	.	.
		Hair loss	Forelimb bilateral	.	X	X	X	X	X	X	X	X
		Scheduled sacrifice		.	.	.	.	.	.	.	.	X

Nominal Dose: Group 1 – 175 mg/kg Group 2 – 550 mg/kg Group 3 – 1750 mg/kg
Group 4 – 5000 mg/kg Group 5 - 1750 mg/kg Group 6 – 5000 mg/kg
Group 7 – 1750 mg/kg Group 8 - 5000 mg/kg

Individual Clinical Observations

Day numbers relative to Start Date

Group Sex	Animal Number	Clinical Sign	Site	-1 A	0 A	0 Ts1	0 Ts2	0 Ts3	1 A	2 A	3 A	4 A	5 A
2f	1585	No Abnormalities Detected		X	X	X	X	.	X	X	X	X	X
		Posture - high		.	.	.	.	X	.	.	.	.	.
		Scheduled sacrifice		.	.	.	.	.	.	.	.	.	.

(continued)

Group Sex	Animal Number	Clinical Sign	Site	6 A	7 A	8 A	9 A	10 A	11 A	12 A	13 A	14 A
2f	1585	No Abnormalities Detected		X	X	X	X	X	X	X	X	X
		Posture - high		.	.	.	.	.	.	.	.	.
		Scheduled sacrifice		.	.	.	.	.	.	.	.	X

Nominal Dose: Group 1 – 175 mg/kg Group 2 – 550 mg/kg Group 3 – 1750 mg/kg
Group 4 – 5000 mg/kg Group 5 - 1750 mg/kg Group 6 – 5000 mg/kg
Group 7 – 1750 mg/kg Group 8 - 5000 mg/kg

Individual Clinical Observations

Day numbers relative to Start Date

Group Sex	Animal Number	Clinical Sign	Site	-1 A	0 A	0 Ts1	0 Ts2	0 Ts3	1 A	2 A	3 A	4 A	5 A
3f	1649	No Abnormalities Detected		X	X	X	.	.	.	X	X	X	X
		Stained skin/fur - brown	Abdomen	.	.	.	.	.	X	.	.	.	.
		Stained skin/fur - brown	Chin	.	.	.	.	X	X	.	.	.	.
		Stained skin/fur - brown	Inguen	.	.	.	.	.	X	.	.	.	.
		Stained skin/fur - brown	Perinasal	.	.	.	.	X	.	.	.	.	.
		Stained skin/fur - brown	Perineum	.	.	.	.	.	X	.	.	.	.
		Wet fur	Inguen	.	.	.	X	X	.	.	.	.	.
		Wet fur	Perineum	.	.	.	X	X	.	.	.	.	.
		Scheduled sacrifice		.	.	.	.	.	.	.	.	.	.

(continued)

Group Sex	Animal Number	Clinical Sign	Site	6 A	7 A	8 A	9 A	10 A	11 A	12 A	13 A	14 A
3f	1649	No Abnormalities Detected		X	X	X	X	X	X	X	X	X
		Stained skin/fur - brown	Abdomen	.	.	.	.	.	.	.	.	.
		Stained skin/fur - brown	Chin	.	.	.	.	.	.	.	.	.
		Stained skin/fur - brown	Inguen	.	.	.	.	.	.	.	.	.
		Stained skin/fur - brown	Perinasal	.	.	.	.	.	.	.	.	.
		Stained skin/fur - brown	Perineum	.	.	.	.	.	.	.	.	.
		Wet fur	Inguen	.	.	.	.	.	.	.	.	.
		Wet fur	Perineum	.	.	.	.	.	.	.	.	.
		Scheduled sacrifice		.	.	.	.	.	.	.	.	X

Nominal Dose: Group 1 – 175 mg/kg Group 2 – 550 mg/kg Group 3 – 1750 mg/kg
Group 4 – 5000 mg/kg Group 5 - 1750 mg/kg Group 6 – 5000 mg/kg
Group 7 – 1750 mg/kg Group 8 - 5000 mg/kg

Individual Clinical Observations

Day numbers relative to Start Date

Group Sex	Animal Number	Clinical Sign	Site	-1 A	0 A	0 Ts1	0 Ts2	0 Ts3	1 A	2 A	3 A	4 A	5 A
4f	1651	No Abnormalities Detected		X	X	X	.	.	.	.	.	.	.
		Lethargic		.	.	.	.	.	X	.	.	.	.
		Stained skin/fur - brown	Chin	.	.	.	.	.	X	.	.	.	.
		Stained skin/fur - brown	Face	.	.	.	.	.	X	.	.	.	.
		Stained skin/fur - brown	Perinasal	.	.	.	.	.	X	.	.	.	.
		Stained skin/fur - brown	Perioral	.	.	.	.	.	X	.	.	.	.
		Stained skin/fur - yellow	Abdomen	.	.	.	.	.	X	.	.	.	.
		Stained skin/fur - yellow	Inguen	.	.	.	.	.	X	.	.	.	.
		Stained skin/fur - yellow	Perineum	.	.	.	.	.	X	.	.	.	.
		Wet fur	Abdomen	.	.	.	.	.	X	.	.	.	.
		Wet fur	Inguen	.	.	.	.	.	X	.	.	.	.
		Wet fur	Perineum	.	.	.	X	X	X	.	.	.	.
		Found dead		.	.	.	.	.	.	X	.	.	.

(continued)

Group Sex	Animal Number	Clinical Sign	Site	6 A	7 A	8 A	9 A	10 A	11 A	12 A	13 A	14 A
4f	1651	No Abnormalities Detected		.	.	.	.	.	.	.	.	.
		Lethargic		.	.	.	.	.	.	.	.	.
		Stained skin/fur - brown	Chin	.	.	.	.	.	.	.	.	.
		Stained skin/fur - brown	Face	.	.	.	.	.	.	.	.	.
		Stained skin/fur - brown	Perinasal	.	.	.	.	.	.	.	.	.
		Stained skin/fur - brown	Perioral	.	.	.	.	.	.	.	.	.
		Stained skin/fur - yellow	Abdomen	.	.	.	.	.	.	.	.	.
		Stained skin/fur - yellow	Inguen	.	.	.	.	.	.	.	.	.
		Stained skin/fur - yellow	Perineum	.	.	.	.	.	.	.	.	.
		Wet fur	Abdomen	.	.	.	.	.	.	.	.	.
		Wet fur	Inguen	.	.	.	.	.	.	.	.	.
		Wet fur	Perineum	.	.	.	.	.	.	.	.	.
		Found dead		.	.	.	.	.	.	.	.	.

Nominal Dose: Group 1 – 175 mg/kg Group 2 – 550 mg/kg Group 3 – 1750 mg/kg
Group 4 – 5000 mg/kg Group 5 - 1750 mg/kg Group 6 – 5000 mg/kg
Group 7 – 1750 mg/kg Group 8 - 5000 mg/kg

Individual Clinical Observations

Day numbers relative to Start Date

Group Sex	Animal Number	Clinical Sign	Site	-1 A	0 A	0 Ts1	0 Ts2	0 Ts3	1 A	2 A	3 A	4 A	5 A
5f	1744	No Abnormalities Detected		X	X	X	.	.	.	.	X	X	X
		Stained skin/fur - brown	Face	.	.	.	.	.	X	.	.	.	.
		Stained skin/fur - brown	Perinasal	.	.	.	.	X	X	X	.	.	.
		Stained skin/fur - yellow	Abdomen	.	.	.	.	.	X	.	.	.	.
		Stained skin/fur - yellow	Inguen	.	.	.	.	.	X	.	.	.	.
		Stained skin/fur - yellow	Perineum	.	.	.	.	.	X	X	.	.	.
		Wet fur	Abdomen	.	.	.	.	X	.	.	.	.	.
		Wet fur	Inguen	.	.	.	X	X	.	.	.	.	.
		Wet fur	Perineum	.	.	.	X	X	.	.	.	.	.
		Scheduled sacrifice		.	.	.	.	.	.	.	.	.	.

(continued)

Group Sex	Animal Number	Clinical Sign	Site	6 A	7 A	8 A	9 A	10 A	11 A	12 A	13 A	14 A
5f	1744	No Abnormalities Detected		X	X	X	X	X	X	X	X	X
		Stained skin/fur - brown	Face	.	.	.	.	.	.	.	.	.
		Stained skin/fur - brown	Perinasal	.	.	.	.	.	.	.	.	.
		Stained skin/fur - yellow	Abdomen	.	.	.	.	.	.	.	.	.
		Stained skin/fur - yellow	Inguen	.	.	.	.	.	.	.	.	.
		Stained skin/fur - yellow	Perineum	.	.	.	.	.	.	.	.	.
		Wet fur	Abdomen	.	.	.	.	.	.	.	.	.
		Wet fur	Inguen	.	.	.	.	.	.	.	.	.
		Wet fur	Perineum	.	.	.	.	.	.	.	.	.
		Scheduled sacrifice		.	.	.	.	.	.	.	.	X

Nominal Dose: Group 1 – 175 mg/kg Group 2 – 550 mg/kg Group 3 – 1750 mg/kg
Group 4 – 5000 mg/kg Group 5 - 1750 mg/kg Group 6 – 5000 mg/kg
Group 7 – 1750 mg/kg Group 8 - 5000 mg/kg

Individual Clinical Observations

Day numbers relative to Start Date

Group Sex	Animal Number	Clinical Sign	Site	-1 A	0 A	0 Ts1	0 Ts2	0 Ts3	1 A	2 A	3 A	4 A	5 A
6f	1746	No Abnormalities Detected		X	X	X	.	.	.	.	.	.	.
		Lethargic		.	.	.	.	X	X	.	.	.	.
		Posture - high		.	.	.	.	X	X	.	.	.	.
		Stained skin/fur - brown	Perioral	.	.	.	.	X	X	.	.	.	.
		Wet fur	Abdomen	.	.	.	X	X	X	.	.	.	.
		Wet fur	Inguen	.	.	.	X	X	X	.	.	.	.
		Wet fur	Perineum	.	.	.	X	X	X	.	.	.	.
		Found dead		.	.	.	.	.	X	.	.	.	.

(continued)

Group Sex	Animal Number	Clinical Sign	Site	6 A	7 A	8 A	9 A	10 A	11 A	12 A	13 A	14 A
6f	1746	No Abnormalities Detected		.	.	.	.	.	.	.	.	.
		Lethargic		.	.	.	.	.	.	.	.	.
		Posture - high		.	.	.	.	.	.	.	.	.
		Stained skin/fur - brown	Perioral	.	.	.	.	.	.	.	.	.
		Wet fur	Abdomen	.	.	.	.	.	.	.	.	.
		Wet fur	Inguen	.	.	.	.	.	.	.	.	.
		Wet fur	Perineum	.	.	.	.	.	.	.	.	.
		Found dead		.	.	.	.	.	.	.	.	.

Nominal Dose: Group 1 – 175 mg/kg Group 2 – 550 mg/kg Group 3 – 1750 mg/kg
Group 4 – 5000 mg/kg Group 5 - 1750 mg/kg Group 6 – 5000 mg/kg
Group 7 – 1750 mg/kg Group 8 - 5000 mg/kg

Individual Clinical Observations

Group Sex	Animal Number	Clinical Sign	Site	Day numbers relative to Start Date: -1 A	0 A	0 Ts1	0 Ts2	0 Ts3	1 A	2 A	3 A	4 A	5 A
7f	1748	No Abnormalities Detected		X	X	X	X	.	X	X	X	X	X
		Wet fur	Inguen	.	.	.	.	X	.	.	.	.	.
		Wet fur	Perineum	.	.	.	.	X	.	.	.	.	.
		Scheduled sacrifice		.	.	.	.	.	.	.	.	.	.

(continued)

Group Sex	Animal Number	Clinical Sign	Site	6 A	7 A	8 A	9 A	10 A	11 A	12 A	13 A	14 A
7f	1748	No Abnormalities Detected		X	X	X	X	X	X	X	X	X
		Wet fur	Inguen	.	.	.	.	.	.	.	.	.
		Wet fur	Perineum	.	.	.	.	.	.	.	.	.
		Scheduled sacrifice		.	.	.	.	.	.	.	.	X

Nominal Dose: Group 1 – 175 mg/kg Group 2 – 550 mg/kg Group 3 – 1750 mg/kg
Group 4 – 5000 mg/kg Group 5 - 1750 mg/kg Group 6 – 5000 mg/kg
Group 7 – 1750 mg/kg Group 8 - 5000 mg/kg

Individual Clinical Observations

Day numbers relative to Start Date

Group Sex	Animal Number	Clinical Sign	Site	-1 A	0 A	0 Ts1	0 Ts2	0 Ts3	1 A	2 A	3 A	4 A	5 A
8f	1975	No Abnormalities Detected		X	X	.	.	.	.	.	.	.	.
		Discharge - clear	Eye bilateral	.	.	.	X	.	.	.	.	.	.
		Lethargic		.	.	X	.	.	.	.	.	.	.
		Prostrate		.	.	.	X	.	.	.	.	.	.
		Salivation		.	.	.	X	.	.	.	.	.	.
		Stained skin/fur - yellow	Perineum	.	.	.	X	.	.	.	.	.	.
		Wet fur	Chin	.	.	.	X	.	.	.	.	.	.
		Wet fur	Perineum	.	.	.	X	.	.	.	.	.	.
		Partially closed	Bilateral	.	.	.	X	.	.	.	.	.	.
		Found dead		.	.	.	.	X	.	.	.	.	.

(continued)

Group Sex	Animal Number	Clinical Sign	Site	6 A	7 A	8 A	9 A	10 A	11 A	12 A	13 A	14 A
8f	1975	No Abnormalities Detected		.	.	.	.	.	.	.	.	.
		Discharge - clear	Eye bilateral	.	.	.	.	.	.	.	.	.
		Lethargic		.	.	.	.	.	.	.	.	.
		Prostrate		.	.	.	.	.	.	.	.	.
		Salivation		.	.	.	.	.	.	.	.	.
		Stained skin/fur - yellow	Perineum	.	.	.	.	.	.	.	.	.
		Wet fur	Chin	.	.	.	.	.	.	.	.	.
		Wet fur	Perineum	.	.	.	.	.	.	.	.	.
		Partially closed	Bilateral	.	.	.	.	.	.	.	.	.
		Found dead		.	.	.	.	.	.	.	.	.

Nominal Dose: Group 1 – 175 mg/kg Group 2 – 550 mg/kg Group 3 – 1750 mg/kg
Group 4 – 5000 mg/kg Group 5 - 1750 mg/kg Group 6 – 5000 mg/kg
Group 7 – 1750 mg/kg Group 8 - 5000 mg/kg

Appendix E
Individual Animal Gross Observations

Individual Gross Observations in Female Rats

	FEMALES							
Group:	1	2	3	4	5	6	7	8
Dose (mg/kg):	175	550	1750	5000	1750	5000	1750	5000
LIVER;								
Discoloration; dark								1975
LUNGS;								
Discoloration; dark								1975
Discoloration; red						1746		
Discoloration; red; diffuse				1651				
MANDIBULAR LYMPH NODE;								
Discoloration; dark; bilateral						1746		
GROSS FINDINGS;								
No Visible Lesions	1581	1585	1649		1744		1748	